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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,953	04/19/2002	C. Frank Bennett	ISPH-0621	3434

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MARSHALL, GERSTEIN & BORUN
6300 SEARS TOWER
233 SOUTH WACKER DRIVE
CHICAGO, IL 60606-6357

EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,953	BENNETT ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *50-69 and 71-74* is/are allowed.

6)☒ Claim(s) *31-34, 36-49* is/are rejected.

7)☒ Claim(s) *35 and 70* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/19/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

In response to the restriction requirement of 9/23/2004, applicants canceled claims 1-30 and added add new claims 31-74, which are directed to compositions corresponding to Group I of the restriction requirement. Applicants also elect SEQ ID NO: 256 for examination.

Priority

This application, filed 4/19/2002, is a 371 of PCT/US00/14471, filed 5/25/2000, which is a CIP of 09/326,186 (U.S. Patent 6,319,906), filed 6/4/1999, which is a CIP of 08/777,266 (U.S. Patent 6, 077,833), filed 12/31/1996. However, SEQ ID NO: 256, from which all the instant claims depend, was not disclosed until the instant application (PCT/US00/14471). Hence, the instant invention is granted a priority date of 5/25/2000.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-34, and 36-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antisense compound comprising SEQ ID NO: 256, does not reasonably provide enablement for any antisense compound comprising at least 8 nucleobases of SEQ ID NO: 256. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The only disclosed use for the claimed antisense compounds is the modulation of B7 mRNA expression. Therefore, the claims will be read as antisense compounds for modulation of B7 expression.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. The art concerning modulation of B7-2 expression (or B7 mRNA in general) with any antisense oligonucleotide based on any 8-base sequence of SEQ ID NO: 256 is unpredictable. Applicants own disclosure demonstrates that whereas some antisense oligonucleotides directed to the B7-2 5' UTR (the location of SEQ ID NO: 256) modulate mRNA expression, others do not. Compare SEQ ID NOs 7, 8, 10, and 16 in Table 5, column 36 of U.S. patent 6,319,906 ('906 hereafter). Derivates of SEQ ID NO: 16 were also unpredictable in their

B7-2 modulation activity: two modulated expression whereas five others had no affect (See Fig. 4 and column 37, lines 19-25). Of the two antisense oligonucleotides that showed activity, one, termed ISIS 10996, was modified chemically to have 2' methoxy substitutions in an attempt to increase the affinity of the oligo for the target RNA. However, this did not lead to increased modulation of B7-2 expression (see column 37, line 27- column 38, line 20). Additionally, SEQ ID NO: 256 is directed to human B7-2 and modulates expression of the corresponding mRNA, but it is unclear how this sequence could modulate other B7 mRNAs (i.e. B7-1) as claimed.

In general, selecting antisense compounds with a physiological function frequently produces results that are "highly variable", "non-informative", or "unreproducible" (see p. 3161, col. 2, 1st full paragraph of Gerwitz et al, 1996). Gerwitz also states that targeting mRNA is a "hit or miss process" in which addition of an antisense oligonucleotide in many experiments "yields no effect on expression" (p. 3161, paragraph bridging columns 2 and 3). Hoke et al (U.S. patent 5,585,479) teach that effective antisense target sequences must be determined experimentally and that "there are no rational explanations or rules that would predict active (antisense target) sequences".(col. 14, line 65-col. 17, line 7 and col. 16, lines 50-53).

State of the art. The state of the art regarding the production and selection of antisense compounds with physiological function is undeveloped and unpredictable (see the "Unpredictability" section above). The development of the claimed antisense compounds would have to be done empirically.

Number of working examples. Other than the oligonucleotide represented by SEQ ID NO: 256, applicants have provided no working examples of antisense compounds of 8-30

nucleobases in length comprising at least an 8-base portion of SEQ ID NO: 256 that modulate B7-2 mRNA expression.

Amount of guidance. Applicants provide no direction for the claimed antisense compounds other than SEQ ID NO: 256, nor how to overcome art-recognized hurdles (as discussed above in the "Unpredictability" section). The specification requires the skilled artisan to practice trial and error experimentation with an array of antisense oligonucleotides based on SEQ ID NO: 256 to determine which (if any) will modulate B7 expression.

Scope of the invention. The claims are broad in nature and read on any antisense compound of 8-30 nucleotides comprising at least 8 bases of SEQ ID NO: 256.

Nature of the invention. The invention involves the unpredictable art of producing or selecting antisense compounds that modulate expression of a B7-2 mRNA.

Level of skill in the art. While the level of skill in the art is high, the unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Duplicate Claims

Claim 70 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 64. When two claims in an application are duplicates or else are so close in content that they both

cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Allowable Subject Matter

Claim 35 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 50-69, 71-74 are allowed. Relevant prior art is represented by U.S. Patent 6,319,906 (issued to applicants), of which the instant application is a CIP. The claims (particularly 22-37) of '906 disclose antisense oligonucleotides to human B7-2 mRNA and would represent an Obviousness-type Double Patenting rejection, except, as noted above, SEQ ID NO: 256 was not disclosed until the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER